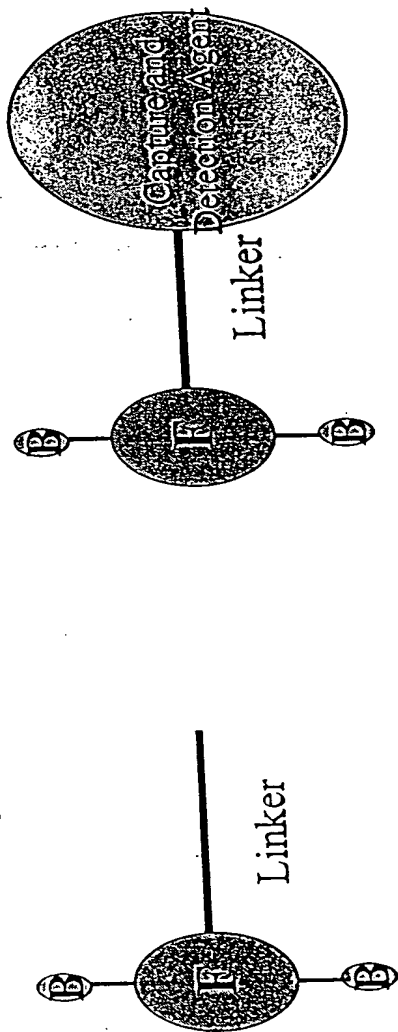


# High-throughput Target ID



## Library of Target ID Compounds

## Library of Bioactive Compounds

Use corresponding activity-based probe to identify the biological target

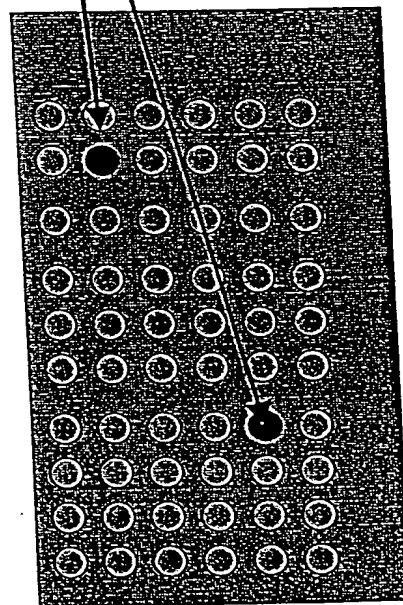


FIGURE 2

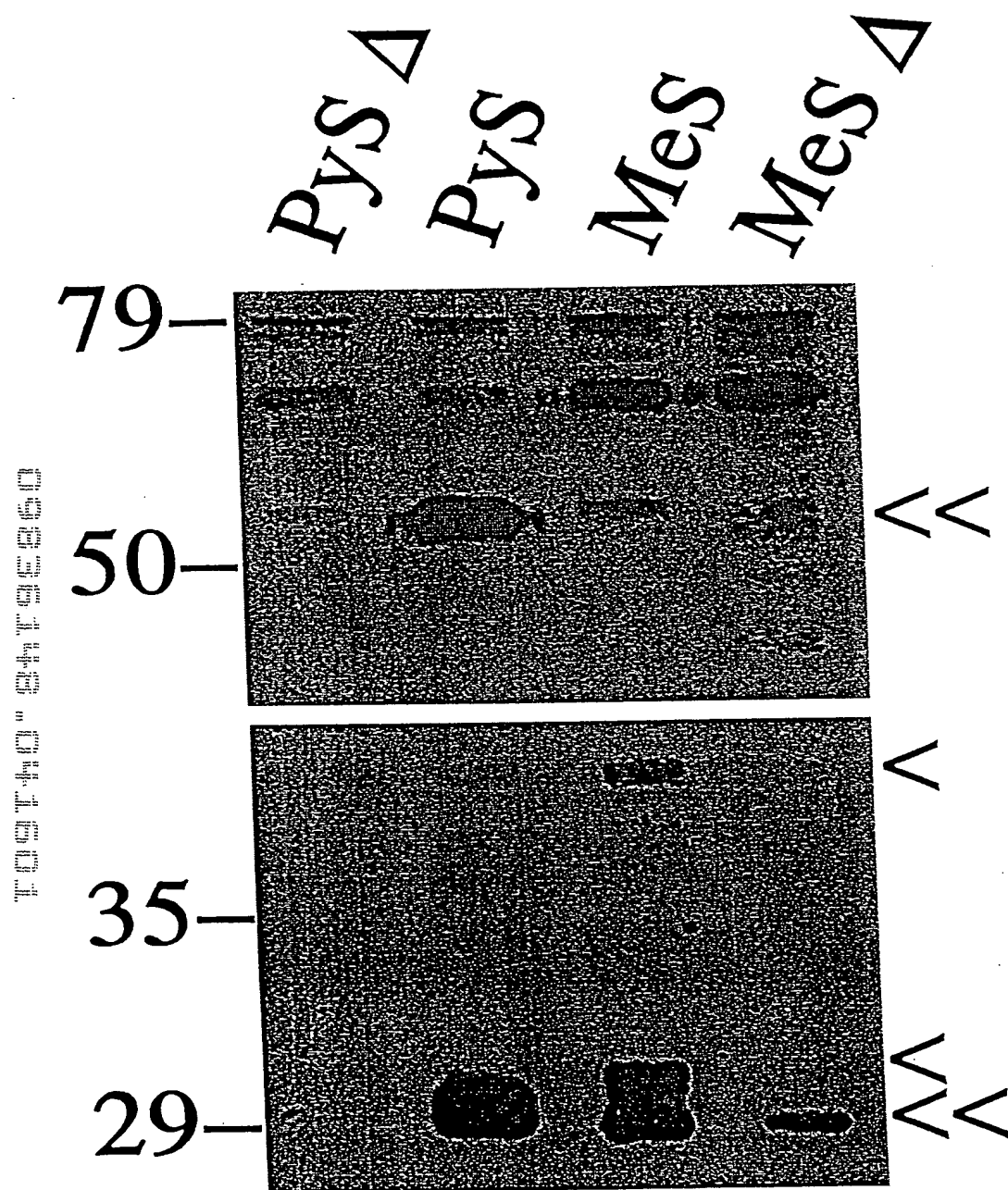
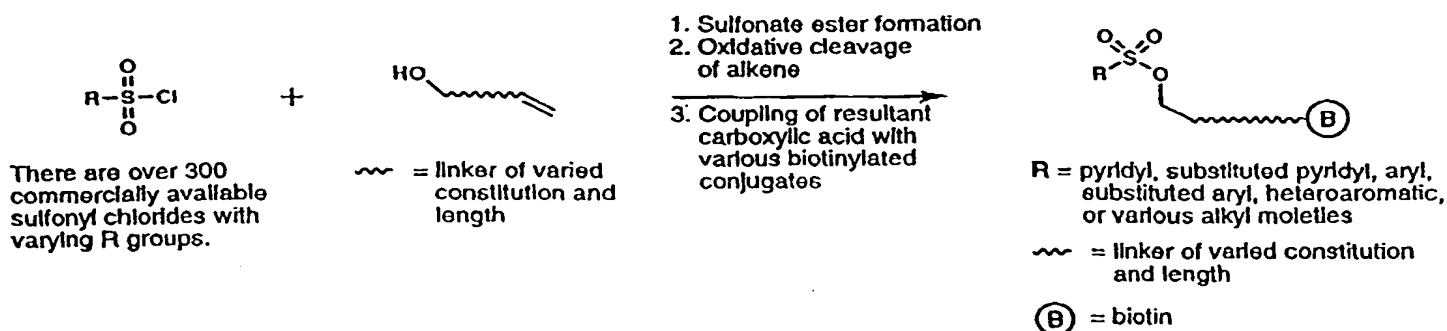
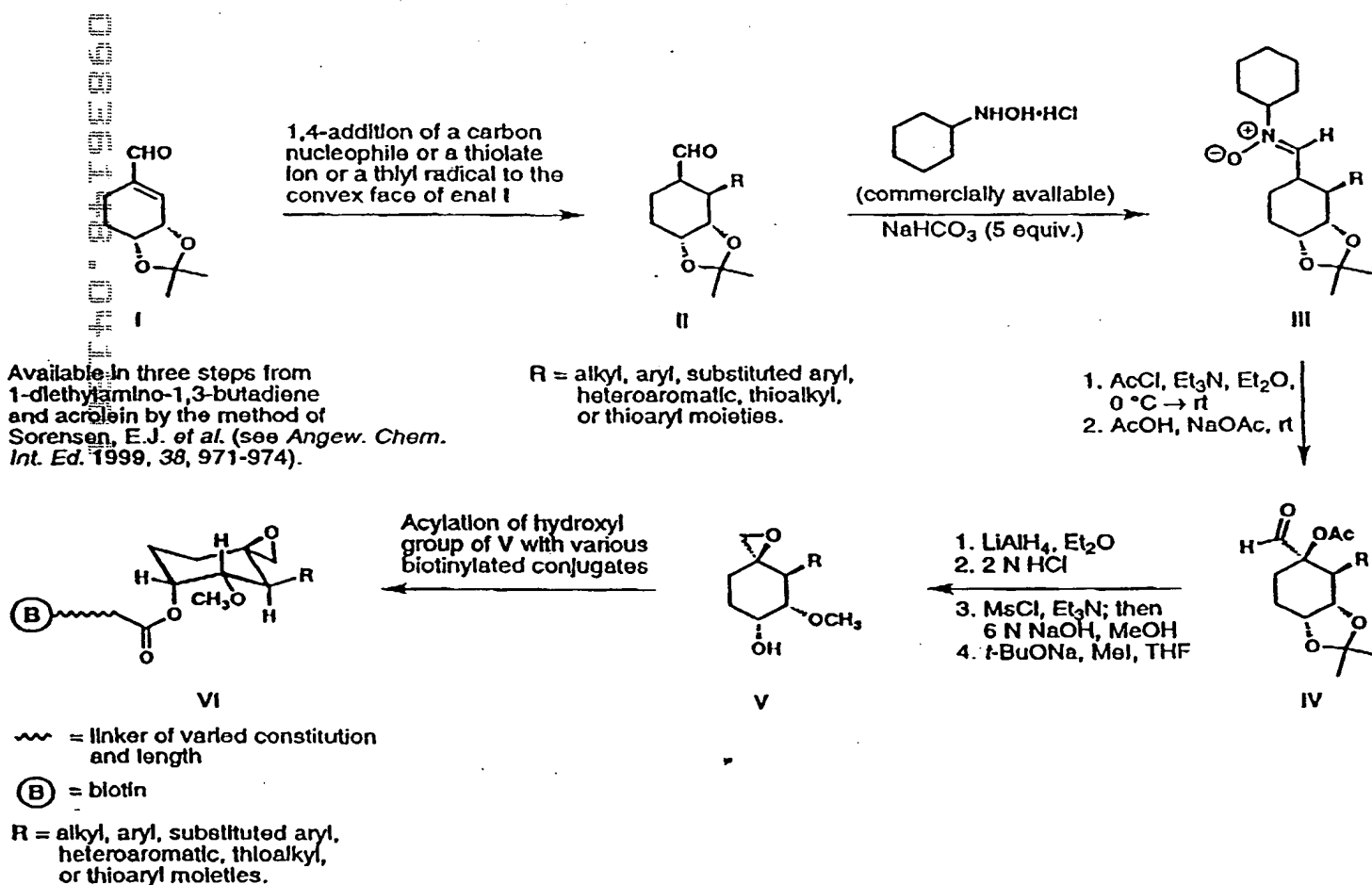




FIGURE 4



Schem 1. A pathway for syntheses of various biotinylated sulfonate esters for use in activity-based proteomics studies.



Scheme 2. A strategy for convergent, stereocontrolled syntheses of conformationally well-defined spiroepoxides of type VI. Literature precedent for I  $\rightarrow$  II  $\rightarrow$  III  $\rightarrow$  IV  $\rightarrow$  V can be found in Sorensen, E.J. *et al.* *Angew. Chem. Int. Ed.* 1999, 38, 971-974. Compounds of type VI are analogs of the m talloprotease (MetAp-2) inhibitor fumagillin and will be employed as covalent affinity agents in activity-based proteomics studies.

# FP-Biotin: a kinetic reporter of SH Activity

- The rates at which the majority of SHs react with FP-biotin can be experimentally followed

FP-biotin readily detects low femtomole quantities of SHs directly in complex cell/tissue proteomes

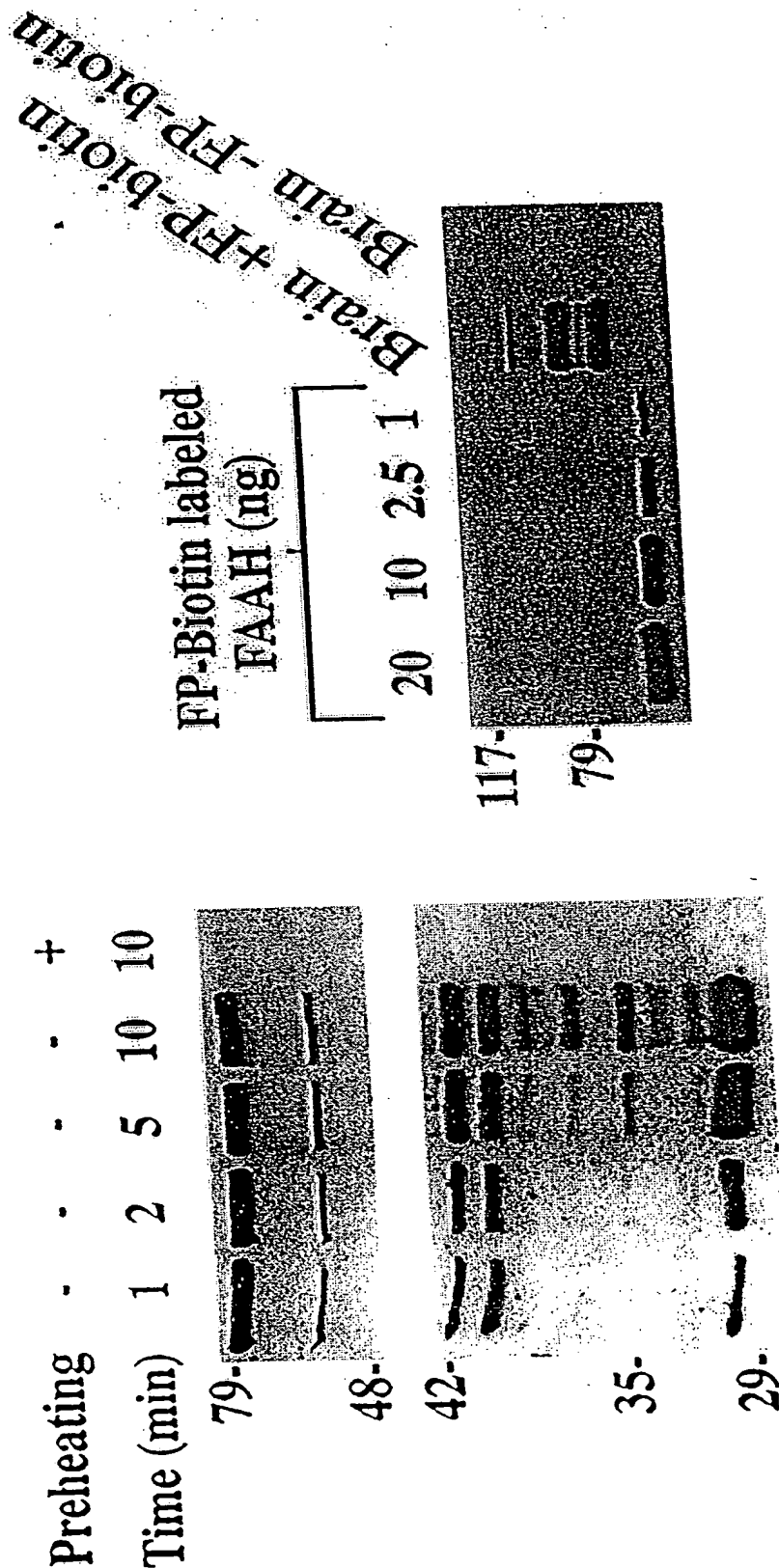


FIGURE 5

# Utility of Multiplexed probes in identifying Serine Hydrolases

Preheating	+	-	-	+
FP-peg-biotin	-	-	+	+
FP-biotin	+	+	-	-

FP-peg-biotin ( $\mu$ M)	4	2	0	2
FP-biotin ( $\mu$ M)	0	2	4	2
Preheated	-	-	-	+

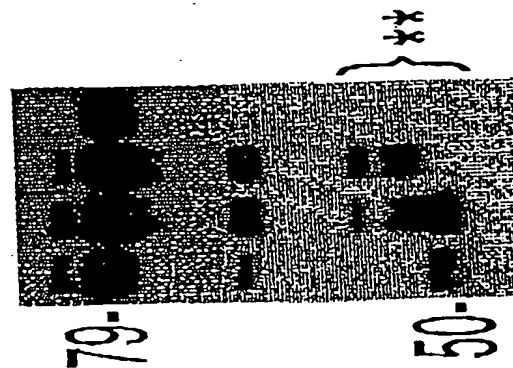
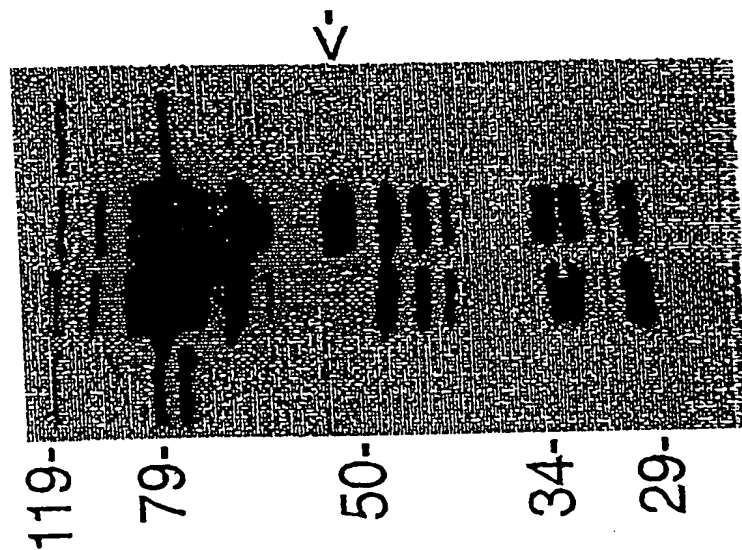


FIGURE 6

FIGURE 7

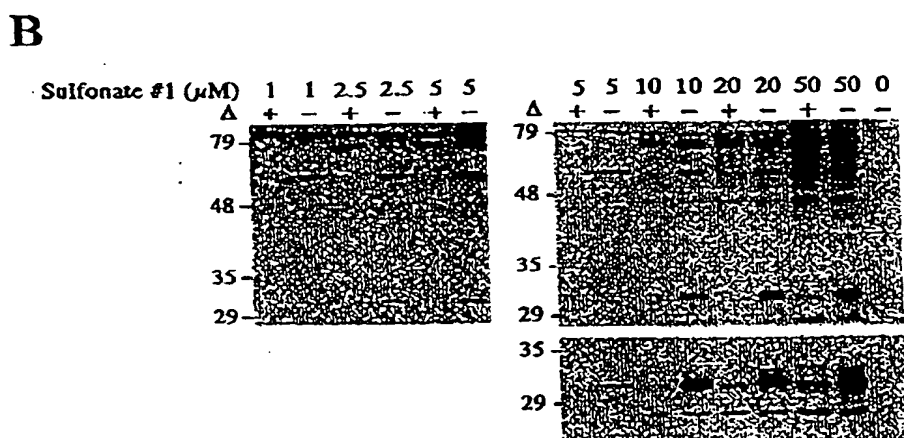
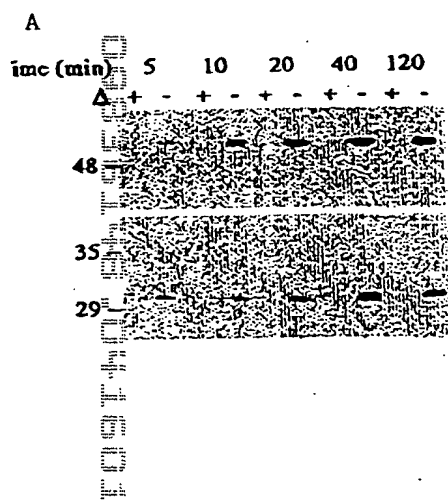
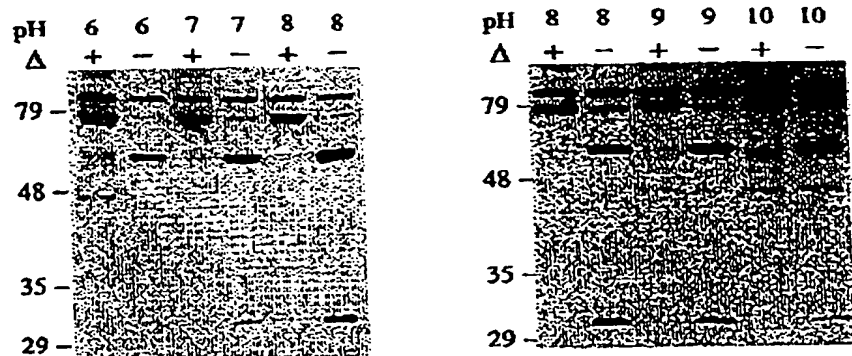
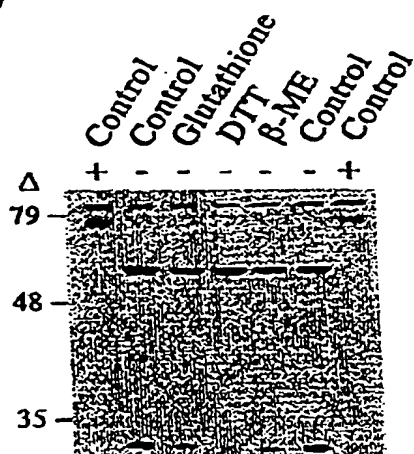


FIGURE 7

C



D



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FIGURE 8

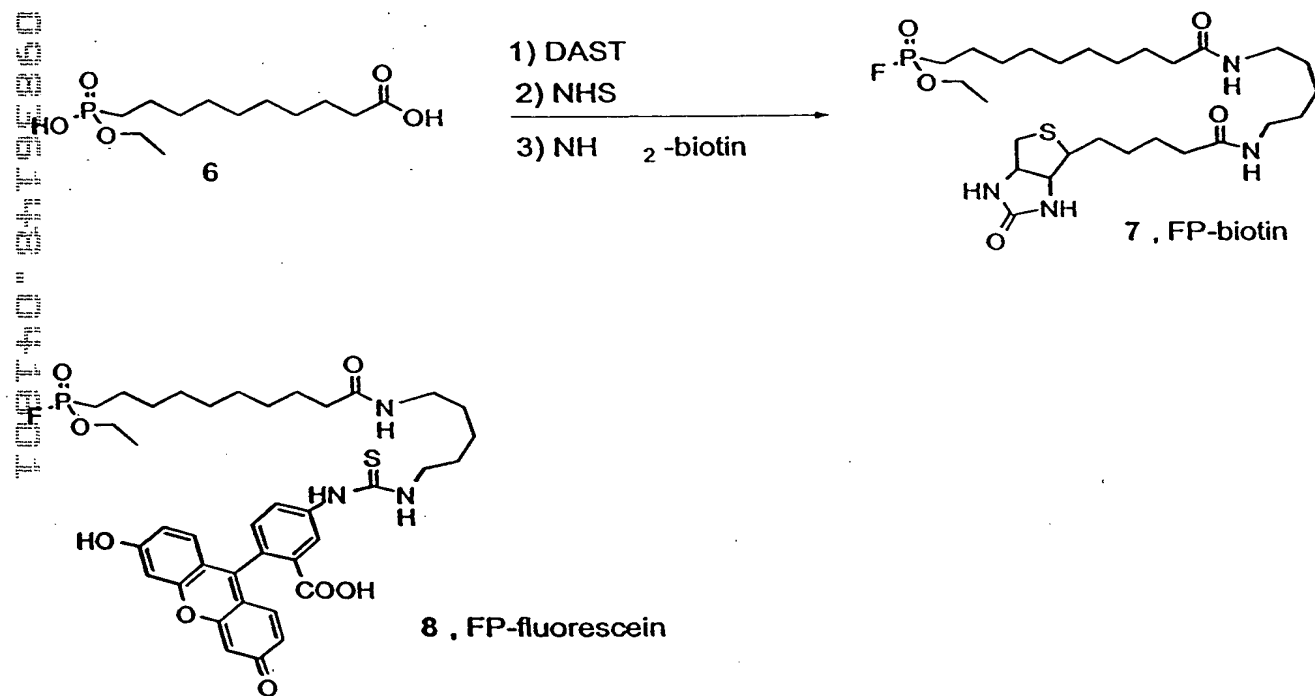
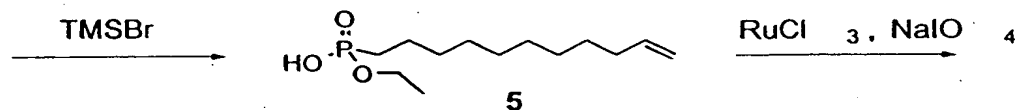
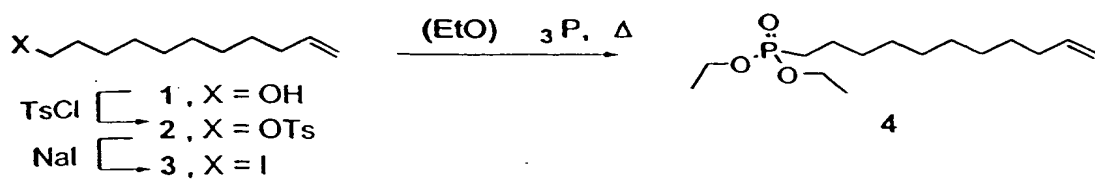
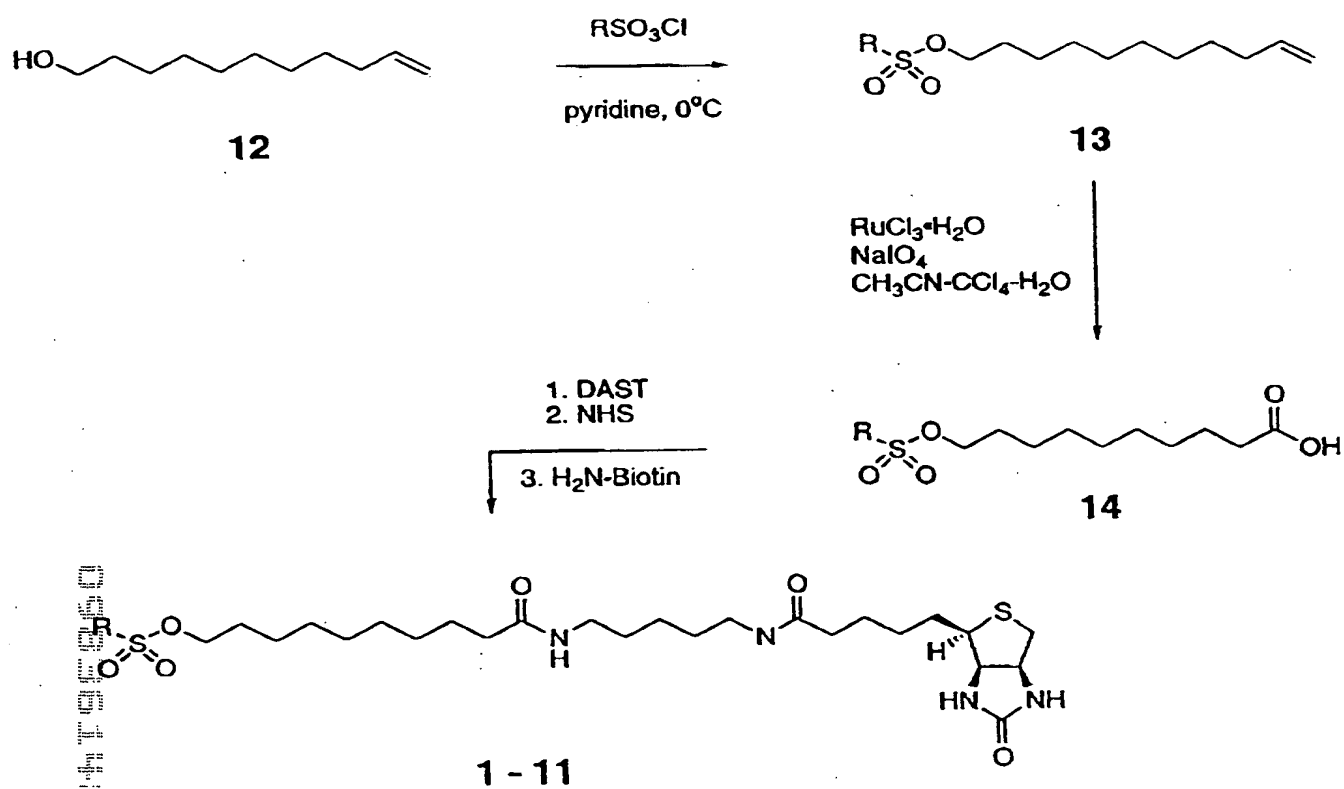


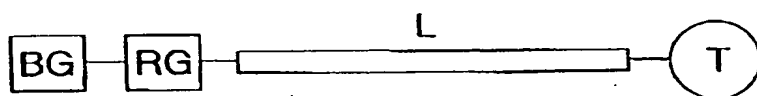
FIGURE 9



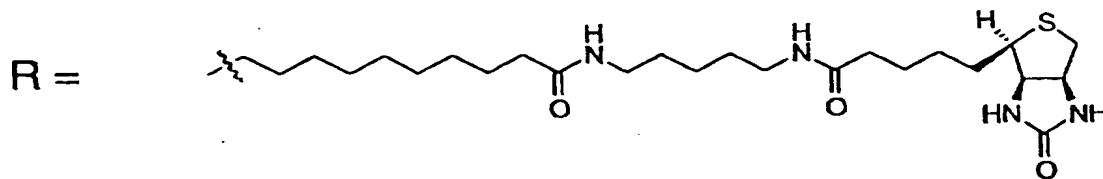
036440-04404

FIGURE 10

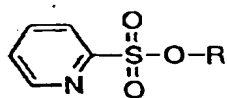
A.



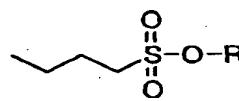
B.



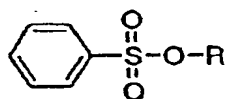
1



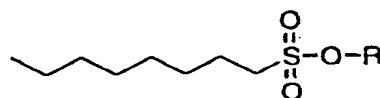
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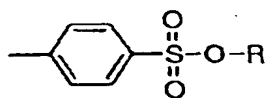
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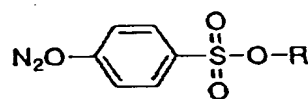
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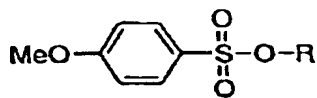
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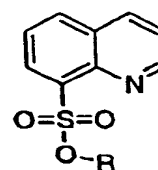
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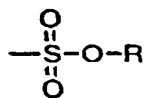
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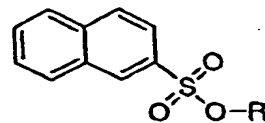
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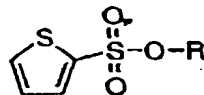
5



10



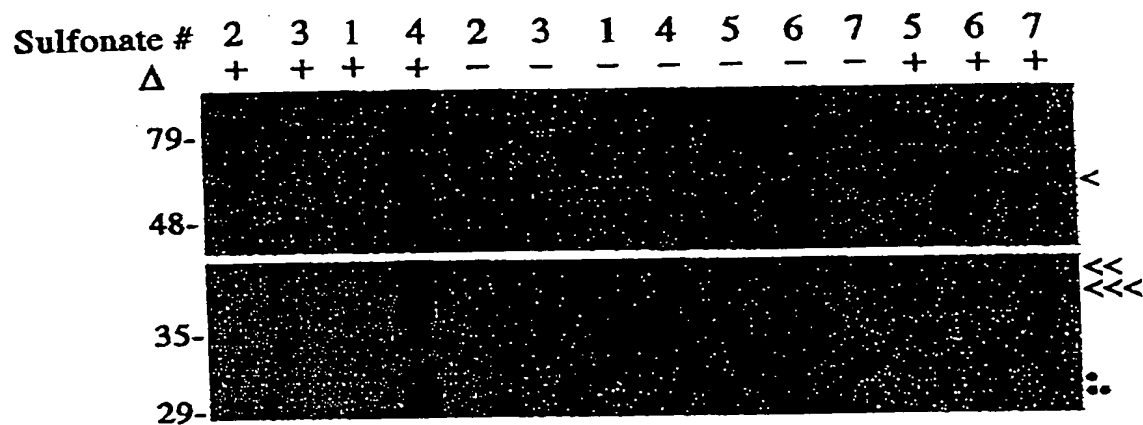
11



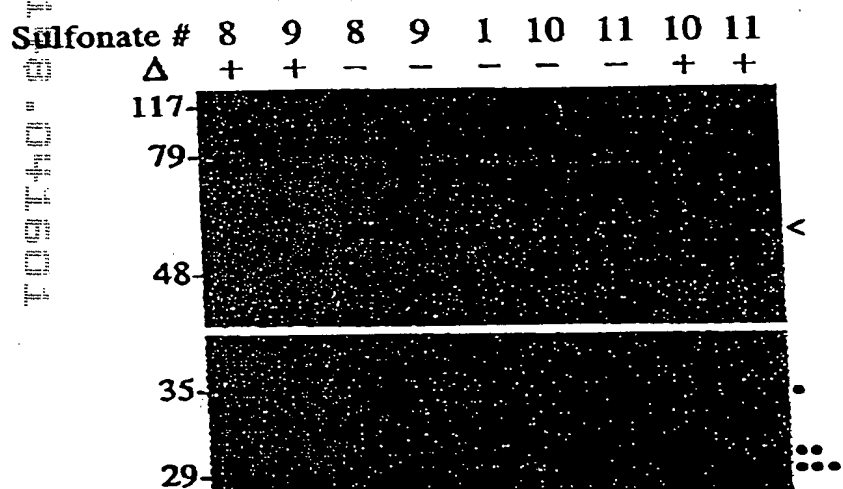
Downloaded from ascelibrary.org by Seattle University on 06/01/15

FIGURE 11

**A**

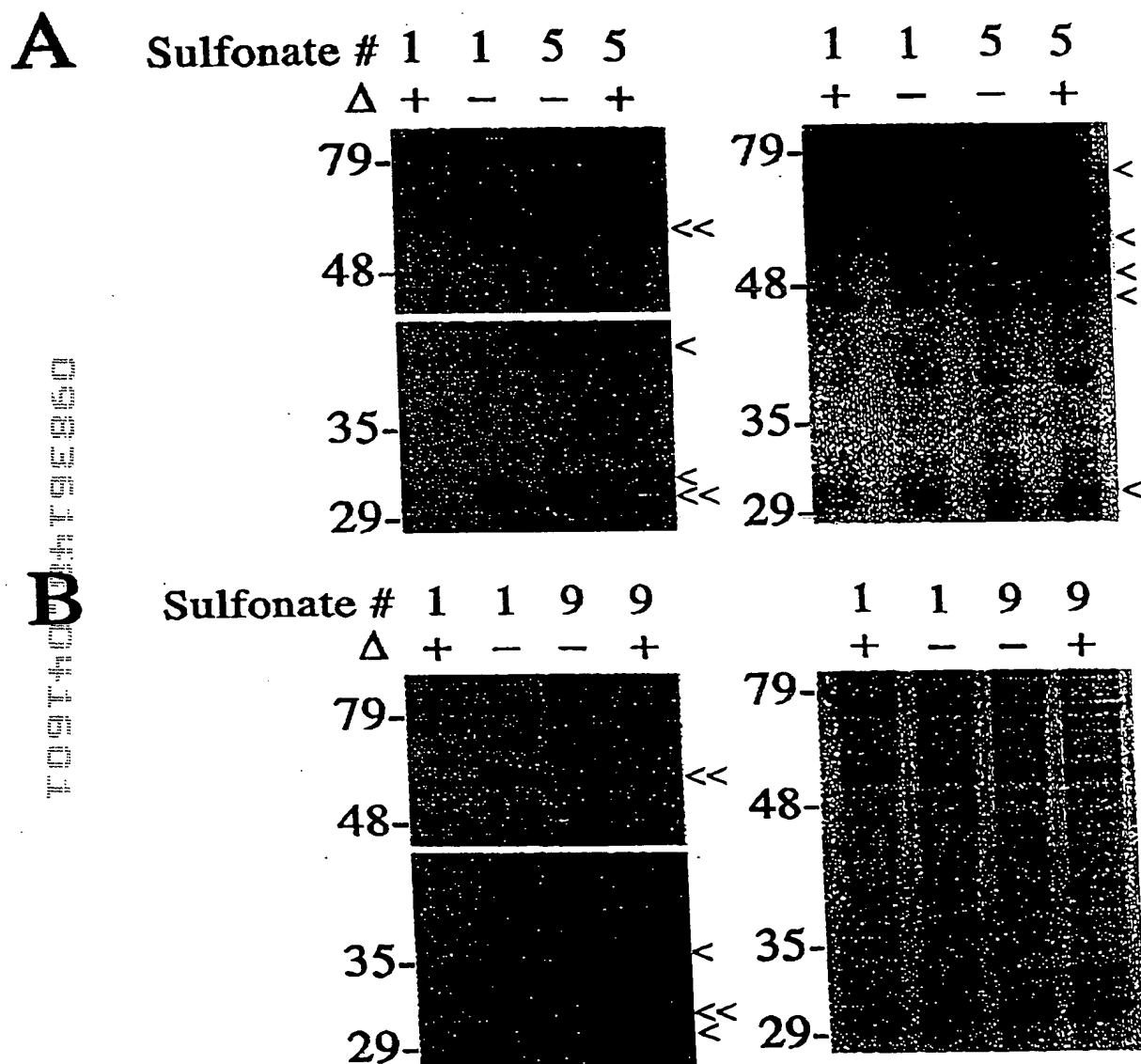


**B**



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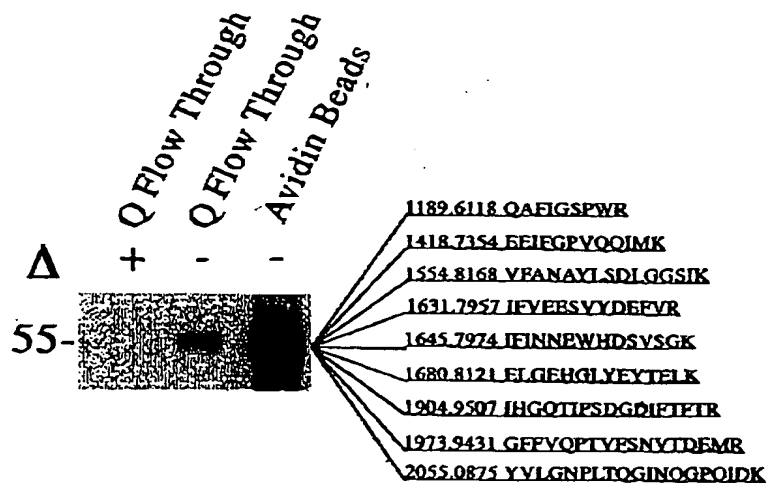
FIGURE 12



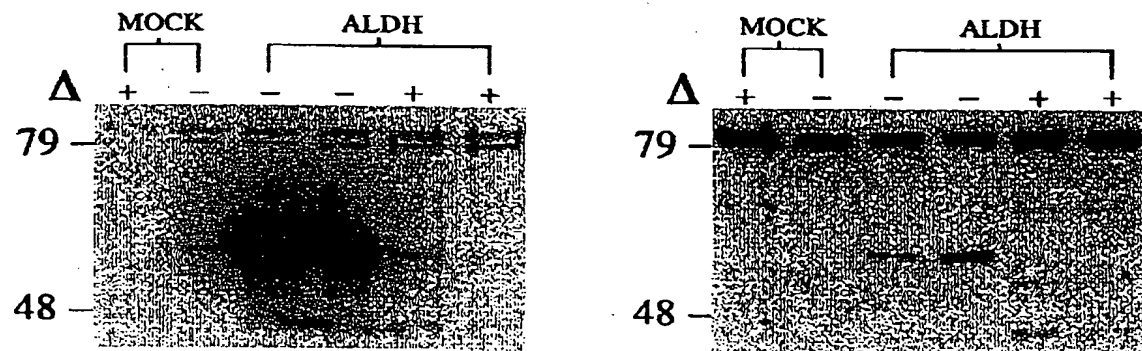
093644041501

A

FIGURE 13



B



C

BL-21 Cells	-	-	+	+
Testis Proteome	+	+	-	-
$\Delta$	+	-	+	-

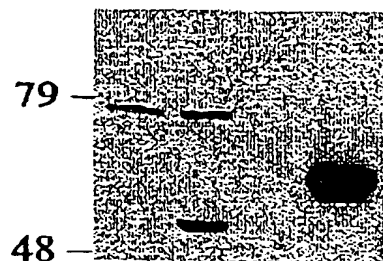
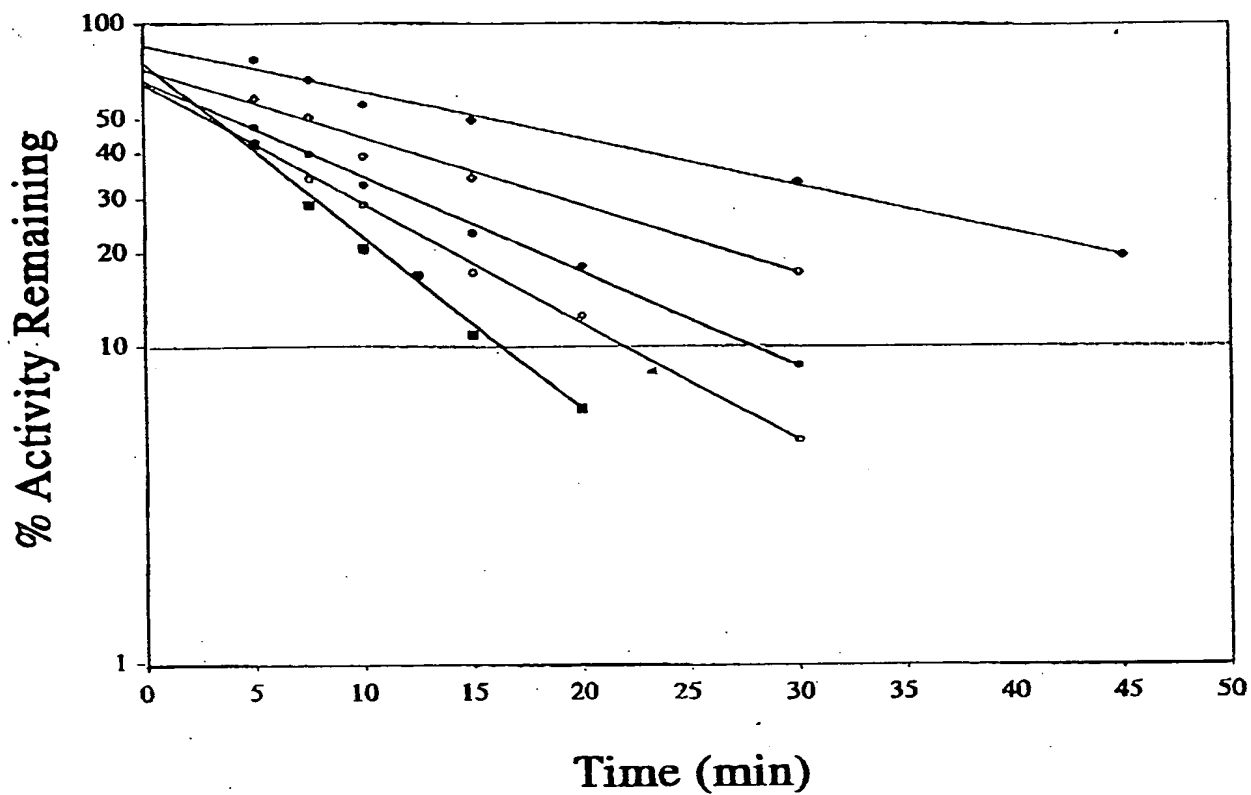


FIGURE 14

A



B

Competitor #	-	-	15	17	16	15	17	16
[Competitor ( $\mu$ M)]	0	0	5	5	5	50	50	50
$\Delta$	+	-	-	-	-	-	-	-

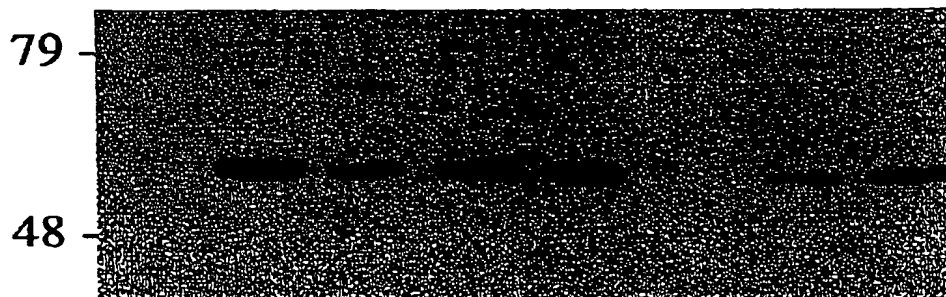
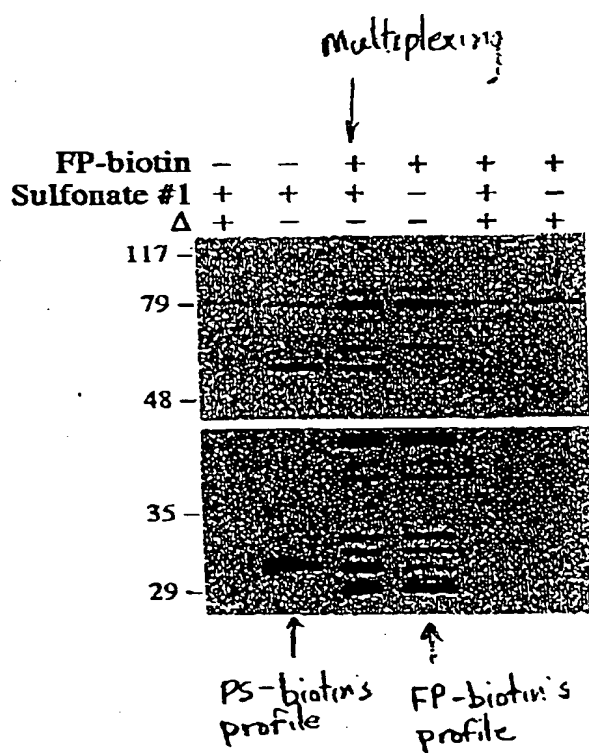


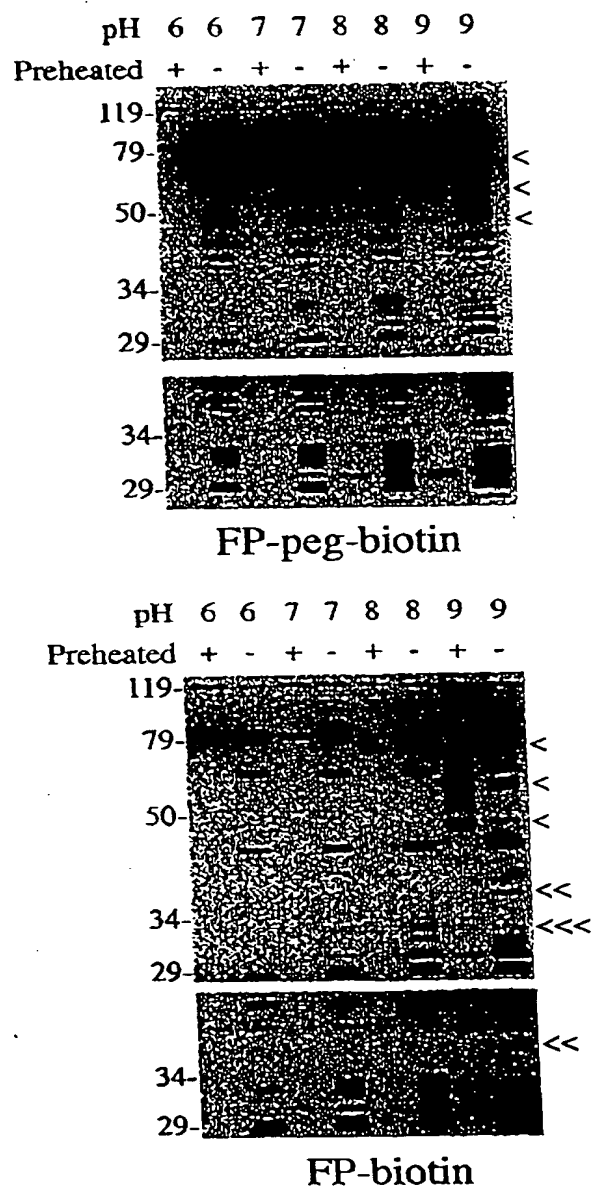
FIGURE 15



0936443-041604



FIGURE 16



0936143-041601

FIGURE 17

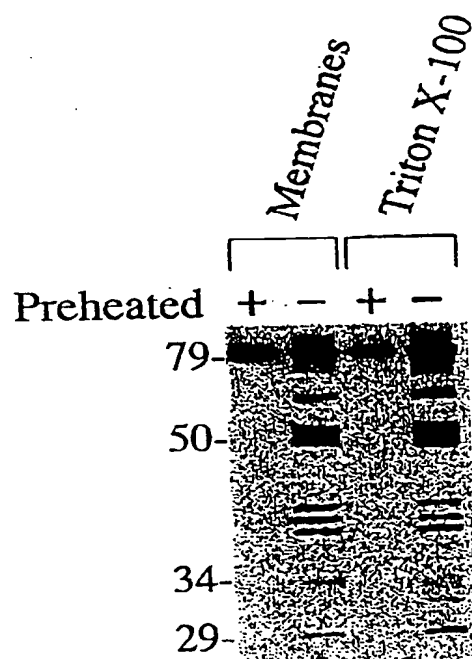
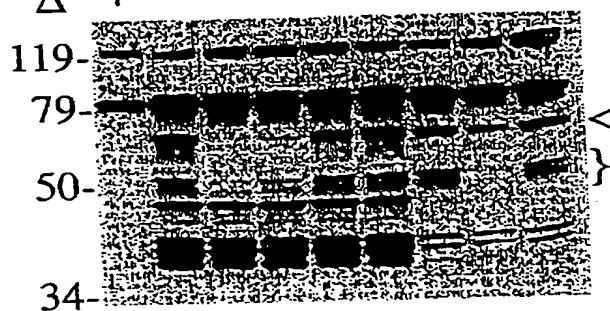


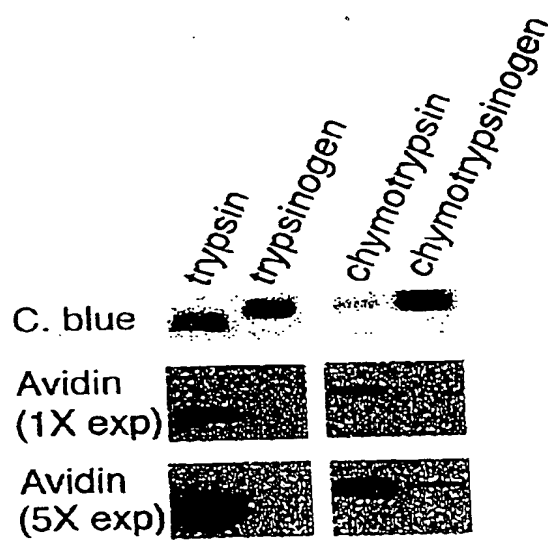
FIGURE 18

FP-peg-biotin	+	+	+	+	+	+	-	-	-
FP-biotin	-	-	-	-	-	-	+	+	+
OTFMK	0	0	200	50	5	1	0	200	50
$\Delta$	+	-	-	-	-	-	-	-	-



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FIGURE 19

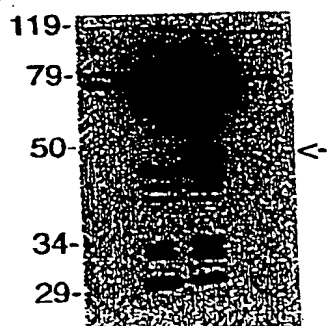


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T09T40-CHT9860

FIGURE 20

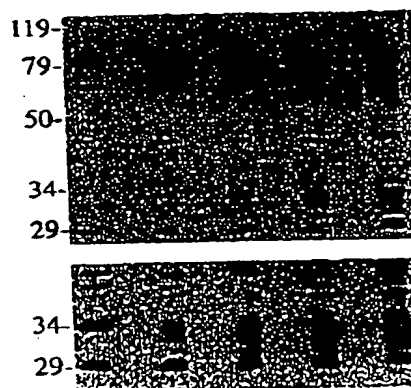
A

FP-peg-biotin	-	-	+	+
FP-biotin	+	+	-	-
Preheated	+	-	-	+



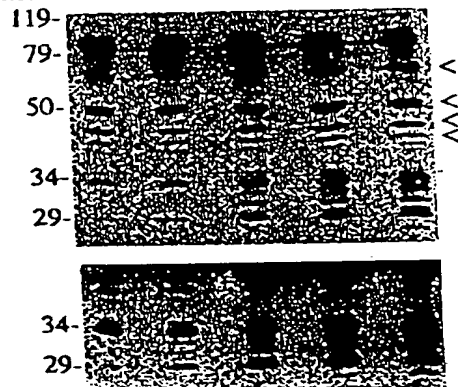
B

FP-biotin ( $\mu$ M)	0.5	1	1	2	2	4	4	8	8
Preheated	-	+	-	+	-	+	-	+	-



C

FP-peg-biotin ( $\mu$ M)	0.5	1	1	2	2	4	4	8	8
Preheated	-	+	-	+	-	+	-	+	-



D

FP-peg-biotin ( $\mu$ M)	1	2	8
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One minute  
reaction

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FIGURE 21

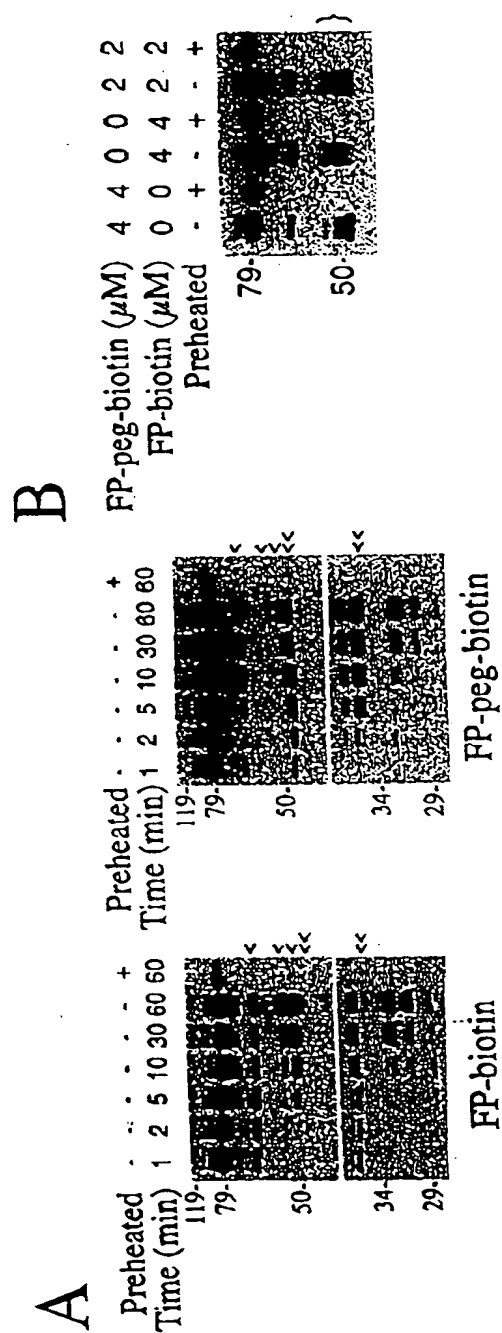
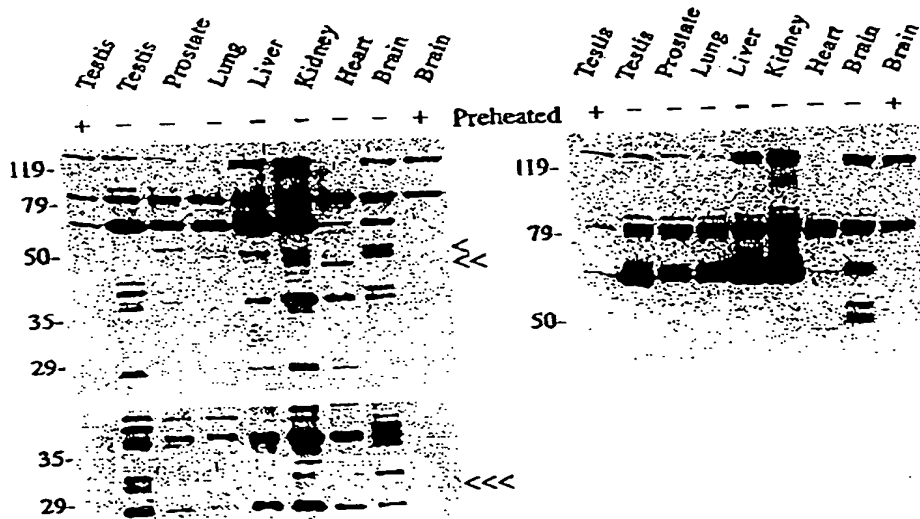


FIGURE 22



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FIGURE 23

